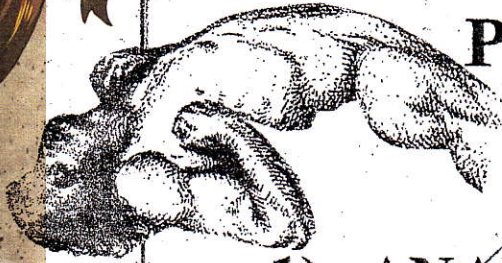


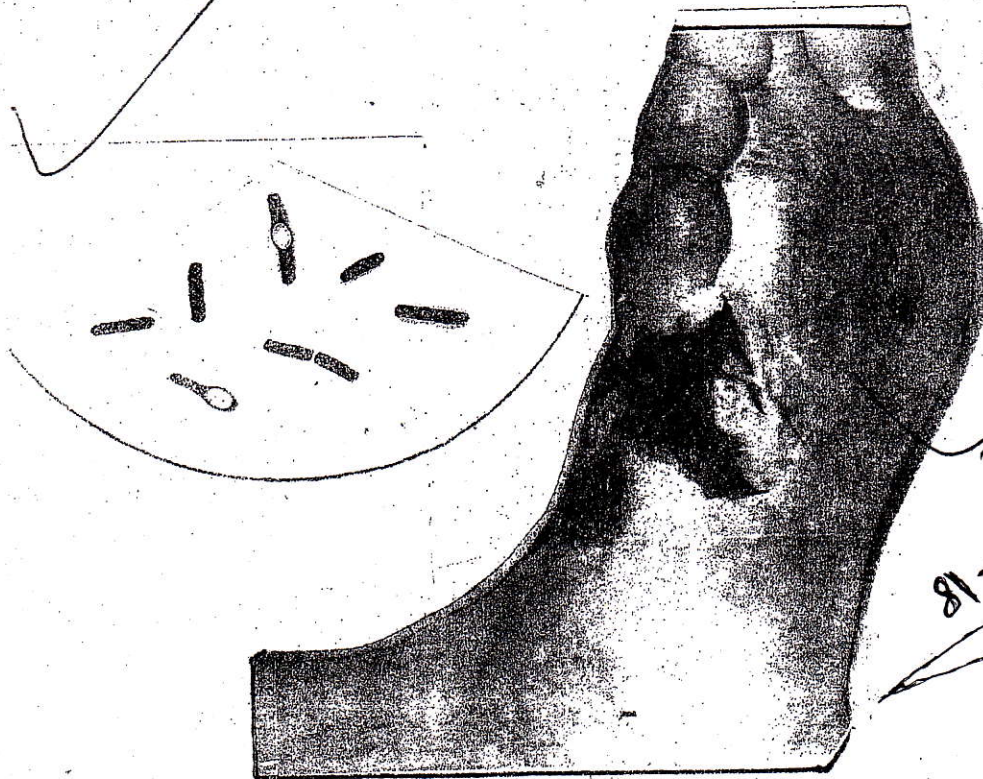
GRAM – POSITIVE RODS.

SPORE – FORMING GRAM- POSITIVE RODS .



1) ANAEROBIC RODS :

GENUS: CLOSTRIDIUM



81-3-2015

DR. A.PROF. NAEEL AHMED BIN AHMED

السلام للخدمات الطلابية

GRAM – POSITIVE RODS

SPORE – FORMING GRAM- POSITIVE RODS .

1) ANAEROBIC RODS :

GENUS: CLOSTRIDIUM .

2) AEROBIC RODS :

GENUS: BACILLUS .

DR. A.PROF. NABEEL AHMED BIN AHMED

الشامل

only Bacillus forming spore

Gauly's Anthrax Clostridia

Aerobic
Anaerobic

Can resist to 100 years.

CLOSTRIDIUM

There are four medically important Clostridium species : C tetani. C botulinum. C perfringens (which causes either gas gangrene or food poisoning). And C difficile. ALL CLOSTRIDIA ARE ANAEROBIC, SPORE - FORMING, GRAM - POSITIVE RODS.

1. Clostridium Tetani → Tetani = Tension = Spasm.

5 μm
x 0.5 μm

Disease C tetani causes TETANUS (LOCKJAW).

Transmission Spores are widespread in soil. The portal of entry is usually a wound site, eg, where a nail penetrates the foot, but the spores also can be introduced during " skin - popping," a technique used by drug addicts to inject drugs into the skin. Germination of spores is favored by necrotic tissue deep, ulcerated, crushed - wounds and poor blood supply in the wound, contaminated with soil and street - dust. Neonatal tetanus, in which the organism enters through a contaminated umbilicus or circumcision wound, is a major problem in some developing countries. Wounds liable to be infected with tetanus:

BACILLI ARE GRAM - STICK - SHAP - ED. SPORES ARE ROUND, TERMINAL

AND PROTECT - ING. 75% and 25%

- car accident wounds, AND BURNS - CASES.
- Wars and earth quacks wounds.
- Gunshot wounds & stab wound.
- Dogs bites.
- Umbilicus and circumcision - contaminated wounds.
- Criminal abortions. → in Home not Hospital.
- And rarely post operative wounds.
- Contaminated Catgut.
- Fireworks - related - tetanus - injuries.
- (i.e. - WI. 1961)

Tetanus neonatorum

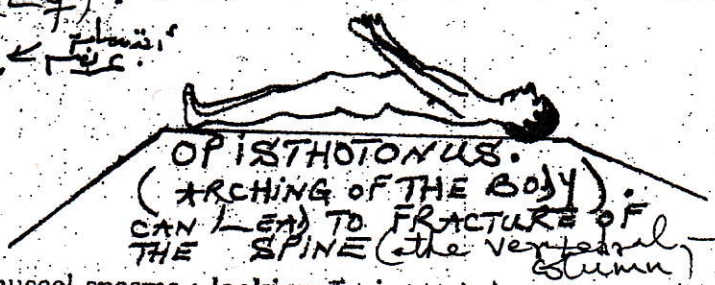
1. Tetanus is a disease of the nervous system.

Pathogenesis Tetanus toxin (tetanospasmin) is an exotoxin produced by vegetative cells at the wound site. This polypeptide toxin is carried intra-axonally (retrograde) to the central nervous system, where it binds to ganglioside receptors and blocks release of inhibitory mediators (eg. glycine) at spinal synapses. Tetanus toxin and botulinum toxin (see below) are among the most toxic substances known. They are proteases that cleave the proteins involved in mediator release. *C. tetani* has little invasive power.

Tetanus toxin has one antigenic type, unlike botulinum toxin, which has eight. There is therefore only one antigenic type of tetanus toxoid in the vaccine against tetanus.



→ laugh (Laf) = *risus*
sardonicus = *risus sardonicus*



OPISTHOTONUS.
(ARCHING OF THE BODY).
CAN LEAD TO FRACTURE OF THE SPINE (the vertebral column).

Clinical Findings Violent muscle spasms; lockjaw (trismus) due to rigid contraction of the jaw muscles, which prevents the mouth from opening; a characteristic grimace known as "*risus sardonicus*"; and exaggerated reflexes occur, respiratory ensues. A high mortality rate is associated with this disease, AS A RESULT OF RESPIRATORY - MUSCLE - SPASM AND OPISTHOTONUS LEADING TO ASPHYXIA AND DEATH.

Laboratory Diagnosis There is no microbiologic or serologic diagnosis. Organisms are rarely isolated from the wound site. *C. tetani* produces a terminal spore, ie, a spore at the end of the rod. This gives the organism the characteristic appearance of a "tennis racket" TOXIN - ANTITOXIN - NEUTRALIZATION REACTION IN 2 MICE IS PERFORMED.

4/1. This allows the excitatory transmitter to stimulate the motor neurons of the spinal cord and of the brain, causing spastic paralysis (rigor).
2/1. The A-subunit is carried by retrograde axonal transport to the C.N.S. where it binds to ganglioside receptors and blocks the release of inhibitory mediators eg. glycine.
2/1. The B-subunit binds to ganglioside receptors on nerve cells.

very difficult to cultivate

Robson cooked meat media
what makes this media anaerobic media?

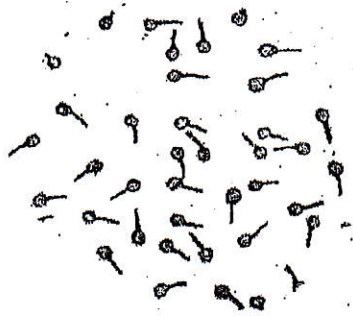
clinically diagnosed

- 1. wound
- 2. Burn
- 3. surgical - surface
- 4. umbilic. - cal - stump

GABA
Panicum
inhibit

Metronidazole
is used

because
Panicum
as
Tetanus spasm

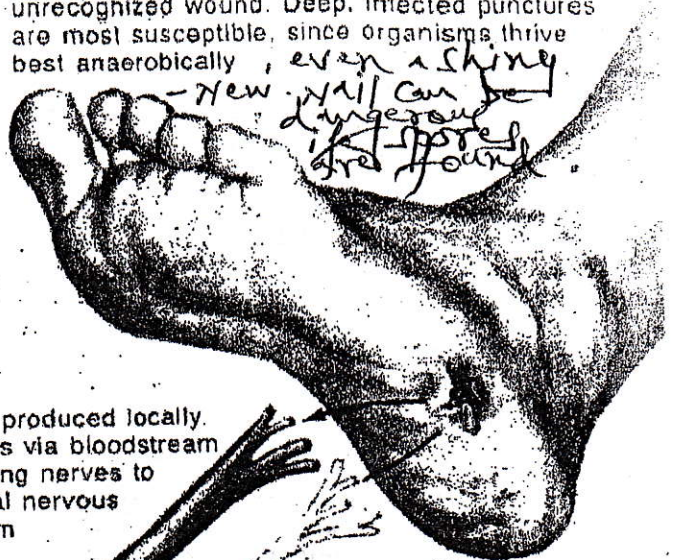


clostr
pos *istridium tetani*: gram-positive, spore-bearing rods

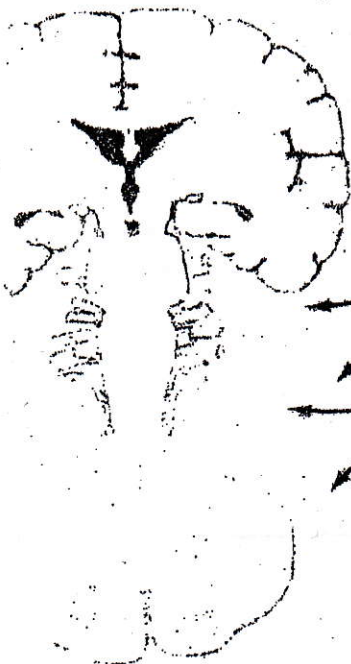
3.1.

Organisms enter through large, small, or even unrecognized wound. Deep, infected punctures are most susceptible, since organisms thrive best anaerobically, even a shiny

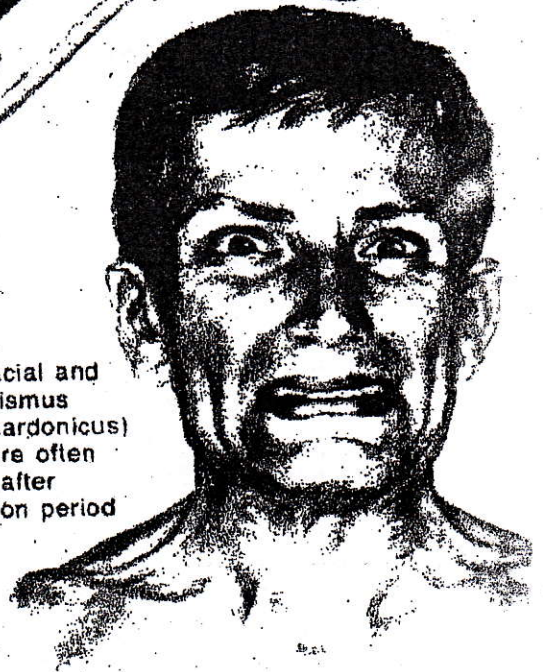
-New nail can be dangerous if not found



Toxin produced locally passes via bloodstream or along nerves to central nervous system

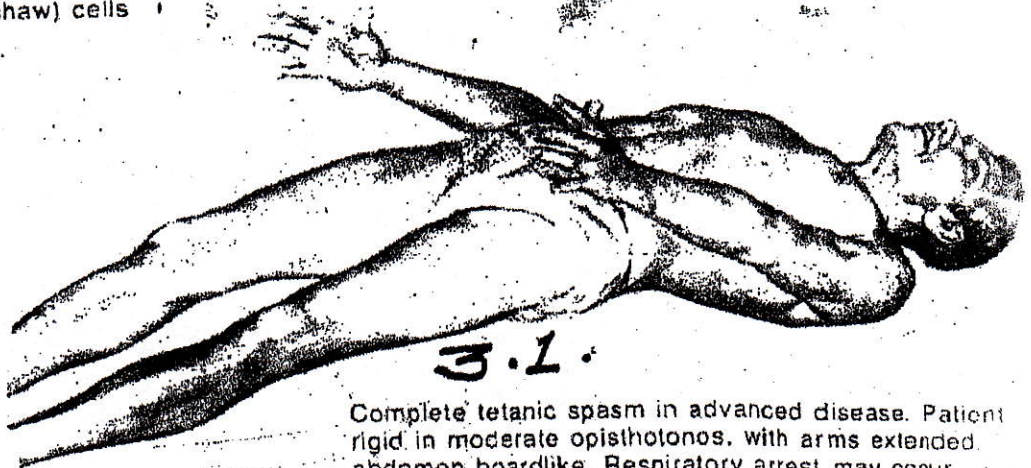


Spasm of jaw, facial and neck muscles (trismus [lockjaw], risus sardonicus) and dysphagia are often early symptoms after variable incubation period



Motor neurons of spinal cord (anterior horn) and of brainstem become hyperactive because toxin specifically attacks inhibitory (Renshaw) cells

beware of shiny nails



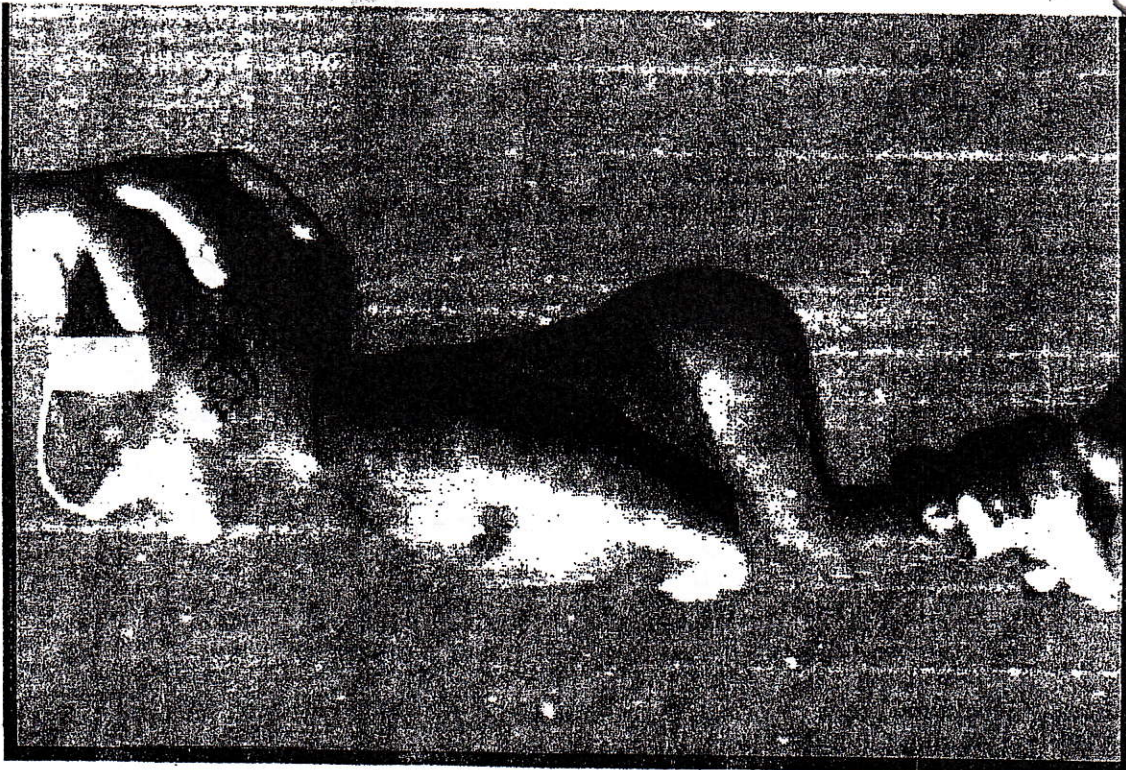
3.1.

Complete tetanic spasm in advanced disease. Patient rigid in moderate opisthotonos, with arms extended, abdomen boardlike. Respiratory arrest may occur

Tox in Aut-toxin
neutralization

MLD minimum little Dose

ATS
postdose



Tetanus 3.2. 90% Mortality
Neonatorum. rate

3.2.

CONFLICTS

becomes activated. Two well-studied toxins of this type are those of diphtheria (see Chapter 20) and cholera.

Diphtheria. The toxin is synthesized as a single polypeptide (from bacteriophage λ genes) and binds by the B subunit to target cells (see Fig. 16.4). Partial cleavage of the polypeptide takes place and then the entire toxin-receptor complex is internalized. The A subunit then splits off and passes into the cytosol, where it inactivates transfer of amino acids from transfer RNA to the polypeptide chain during translation of mRNA by ribosomes. It does this by

catalysing attachment of adenosine diphosphate ribose to the elongation protein (ADP-ribosylation), effectively blocking protein synthesis.

Cholera. Here the toxin is released as a complex of five B subunits surrounding the A subunit. The latter is cleaved into two fragments A1 and A2 held by disulphide bonds. The B subunits bind to ganglioside receptors on intestinal epithelial cells, leading to internalization of the A subunits which then separate from one another (see Fig. 16.4). The A1 portion then ADP-ribosylates one of the regulatory

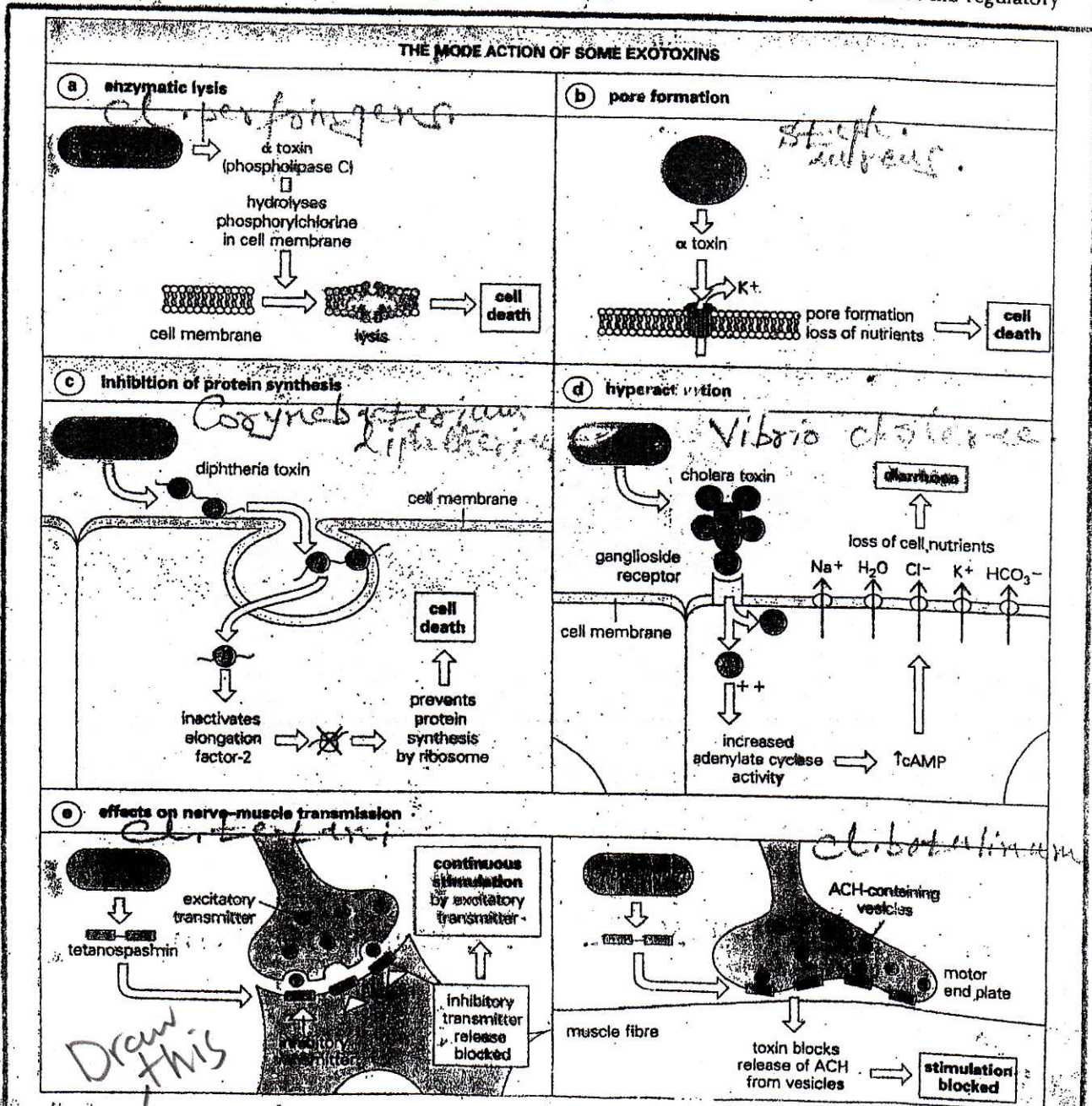


Fig. 16.4 The mode of action of some exotoxins. Bacterial toxins act in a variety of ways. Often the toxin is a two-chain molecule, one chain being concerned with entry into cells while the other has inhibitory activity against some vital function.

Draw all these.

molecules involved in the production of cyclic AMP. As a result the molecule is unable to turn off production. The increased levels of cAMP in the cell change the Na^+/Cl^- flux across the cell membrane, resulting in a massive outflow of water from the cell and causing the profuse diarrhoea of cholera. The exotoxins of *E. coli* and *Salmonella* have similar actions, as does pertussis toxin.

Toxins affecting passage of nerve impulses

The toxins of tetanus and botulism are among the most potent known, one gram of botulinum toxin being sufficient to kill 10 million people! They have the characteristic A + B structure, the B subunit binding to ganglioside receptors on nerve cells. The internalized A subunit of tetanus is carried by axonal transport from the point of production to the CNS, where it interferes with synaptic transmission in inhibitory neurones by blocking neurotransmitter release. This allows the excitatory transmitter to continuously stimulate the motoneurones, causing spastic paralysis. Botulinum toxin enters the body via the intestine, escaping digestion and crossing the gut wall. The toxin affects peripheral nerve endings at the neuromuscular junction, blocking presynaptic release of acetylcholine. This prevents muscle contraction, causing flaccid paralysis.

Diarrhoea

Diarrhoea, is an almost invariable result of intestinal infections and one of the major causes of death in children

world-wide (see Chapter 25). It can be looked at in two ways – as a means for the host to rid itself rapidly of the infectious organism, and as a means for the infection to spread to other hosts.

Diarrhoea is a feature of a wide range of organisms, but in only a few cases is the exact mechanism understood. Damage to the intestinal epithelium is usually the underlying cause, and this may be due directly to infection of the cells (e.g. by rotaviruses) or by the effect of toxins (e.g. cholera, shigella). Many of the organisms causing diarrhoea can be picked up from food, but the term 'food poisoning' is usually reserved for those cases where toxins are already present in the food rather than being generated during the growth of organisms in the intestine. As would be expected, the former causes symptoms earlier, hours after exposure as opposed to days (Fig. 16.5).

PATHOLOGICAL ACTIVATION OF NATURAL IMMUNE MECHANISMS

The very potent natural immune mechanisms discussed in Chapter 12 have in-built safety as far as specificity is concerned. They have had to evolve in the constant presence of the host's 'self' antigens, which they therefore do not respond to. However, they are not so well insured in the quantitative sense, and there are many cases where overactivity in the process of damaging an invading parasite can also damage innocent host tissues.

INFECTIOUS CAUSES OF DIARRHOEA

food poisoning (due to pre-formed toxin in food)		
	onset	source
<i>Staphylococcus aureus</i>	1-6 hrs	cream, meat, poultry
<i>Clostridium perfringens</i>	8-20 hrs	reheated meat
<i>Clostridium botulinum</i>	12-36 hrs	canned food
<i>Bacillus cereus</i>	1-20 hrs	reheated foods
Intestinal infections		
	onset	source
Rotavirus	2-5 days	contact (faecal-oral)
Salmonella	1-2 days	eggs
Shigella	1-4 days	faecal-oral
Campylobacter	1-4 days	poultry, domestic animals
<i>V. cholerae</i>	2 days	faecal-oral
<i>E. coli</i>	1-4 days	traveller's diarrhoea
<i>Yersinia enterocolitica</i>	days-weeks	pets (e.g. dogs)
<i>Giardia lamblia</i>	1-2 weeks	contaminated water
<i>Entamoeba histolytica</i>	days-weeks	
<i>Cryptosporidium</i>	days-weeks	faecal-oral, opportunistic (e.g. in AIDS)
<i>Isospora belli</i>		

Fig. 16.5 Infectious causes of diarrhoea. World-wide infectious diarrhoea is the major cause of infant mortality.

- ① Staph. aureus - food poisoning - source is food-handlers
- ② other organisms causing food poisoning are soil - organisms found in water, faeces and sewage.

3.4.

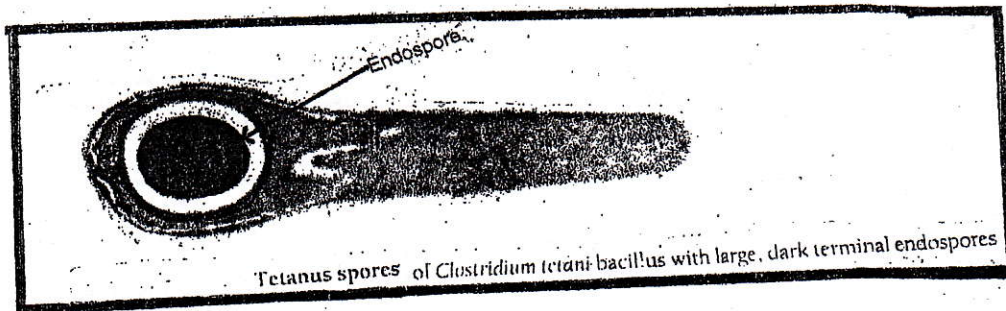
Major salmonella.

A soldier dying of tetanus.



Figure 22.6 An advanced case of tetanus. A drawing of a British soldier during the Napoleonic wars. These spasms, known as opisthotonos, can actually result in a fractured spine. (Drawing by Charles Bell of the Royal College of Surgeons, Edinburgh.)

Tetanus toxin (tetanospasmin) is a neurotoxin that acts on nerves, resulting in the inhibition of muscle relaxation.



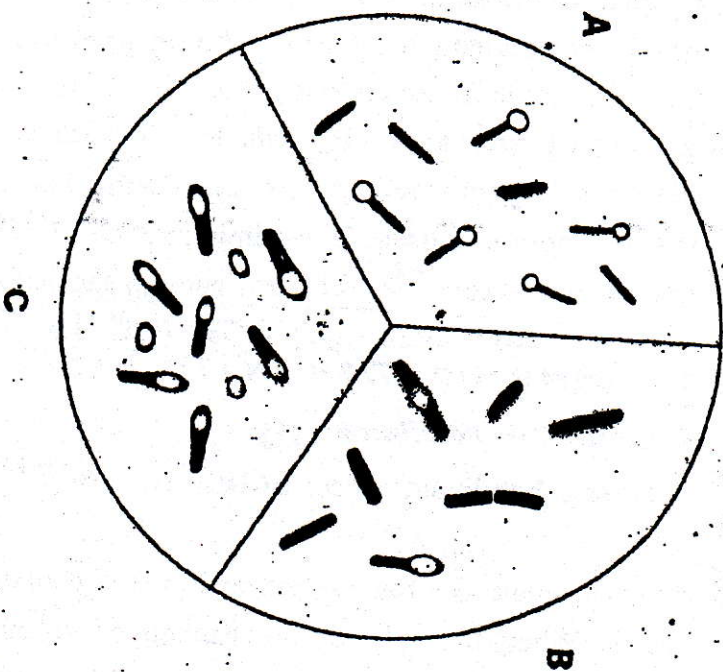


FIG. 16. Clostridia. A, *Clostridium tetani*, sporing ('drumstick') and non-sporing forms. B, *Cl. perfringens* (*Cl. welchii*), sporing forms rarely seen. C, *Cl. sporogenes*.

Treatment Tetanus immune globulin is used. Penicillin G or metronidazole is probably useful. An adequate airway must be maintained and respiratory support given. Benzodiazepines, eg, valium, should be given to prevent spasms.

Prevention Tetanus is prevented by immunization with tetanus toxoid*

Excellent -
Surgical -
Tetanus

(formaldehyde- treated toxin) in childhood and every 10 years thereafter. When trauma occurs, the wound should be cleaned and derided and tetanus toxoid booster should be given. If the wound is grossly contaminated, **tetanus immune globulin**, as well as the toxoid booster, should be given and penicillin administered. Tetanus immune -

HUMAN - Y -

globulin (tetanus antitoxin) is made in humans to avoid serum sickness reactions (anaphylactic shock and death) that occur when antitoxin made in horses is used. The administration of both immune globulins

* at
different
sites
of the
buttocks
to avoid
neutralization
of the
toxoid
by T.I.G.

and tetanus toxoid (*at different sites in the body) is an example of passive - active immunity. **TETANUS IS TOTALLY PREVENTABLE BY IMMUNIZATION WITH D.P.T. VACCINE. + تطعيم الدفتريا**

2. Clostridium botulinum

Disease C botulinum causes **botulism**. = Botulus = sausage.

Transmission Spores, widespread in soil, contaminate vegetables and meats. When these foods are canned or vacuum - packed without adequate sterilization , spores survive and germinate in the anaerobic environment. Toxin is produced within the canned food and ingested **preformed**. The highest - risk foods are (1) alkaline vegetables such as green beans, peppers, and mushrooms and (2) smoked fish. The toxin is relatively heat - labile : it is inactivated by boiling for several minutes. Thus, disease can be prevented by sufficient cooking.

* = in D.P.T. VACCINE.

①. **Clostridium botulinum** produces the most powerful **TOXIN IN NATURE. THE LETHAL DOSE FOR MICE IS 0.000003 mg, i.e 3 mg WILL KILL 30,000,000 MICE WEIGHING 600,000 TONS**

Smoked Fish

small part
of the

Clinical Use of Botulinum Toxin

The powerful effects of the neurotoxins produced by *Clostridium botulinum*, best known as a cause of lethal food poisoning, have been harnessed to help victims of dystonia. Dystonia refers to a group of neurologic disorders characterized by abnormal, sustained involuntary movements, often twisting, that are of unknown origin. In one form, blepharospasm, the patient's eyes remain tightly closed at all times. Physicians inject small quantities of botulinum toxin (trade name, Oculinum A) at several sites around each eye. The toxin blocks nerve impulses to muscles, thereby relieving the spasms of the eyelids [Photos (a) and (b)]. Injections are needed every 2 to 3 months. Some people receive such treatment for 4 to 5 years without problems; others develop antibodies (immune defenses) against the toxin after many injections. Because there are several different types of the toxin, it is hoped that patients can switch to a different form once they develop antibodies against one form. A round of injections can cost from \$400 to \$1800.

A cosmetic use of botulinum toxin, rapidly gaining in favor, is removal of wrinkles, especially "frown" wrinkles in

the center of the forehead. The forehead muscles are injected, become paralyzed in a relaxed state for several months, and cannot pull the skin together into deep creases (Photos (c) and (d)).

Other dystonias being helped by botulinum toxin include oromandibular dystonia, in which the patient's jaws are clenched so tightly that the jaw bones may break, causing midfacial collapse. Eating and speaking are difficult, and some patients starve to death. Vocal cord spasms, causing a cracked tremulous voice, and "stenographers' cramp," causing the middle finger to extend rigidly, are also being treated experimentally with the toxin.

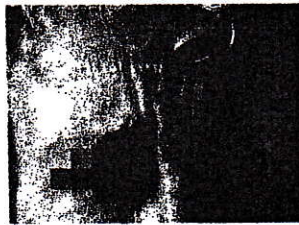
Oculinum A is licensed for treating adults with strabismus (cross-eye, lazy eye). Small amounts are injected into the overcontracted eye muscle, which then relaxes and lengthens. The antagonistic muscles on the other side of the eye contract to take up the slack, and the eye can then look straight ahead.



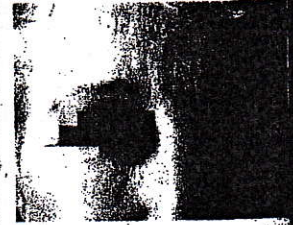
(a)



(b)



(c)



(d)

A patient with hemifacial spasm before (a) and 2 weeks after (b) treatment with botulinum toxin. A patient with forehead "frown" wrinkles before (c) and 2 weeks after (d) treatment with botulinum toxin.

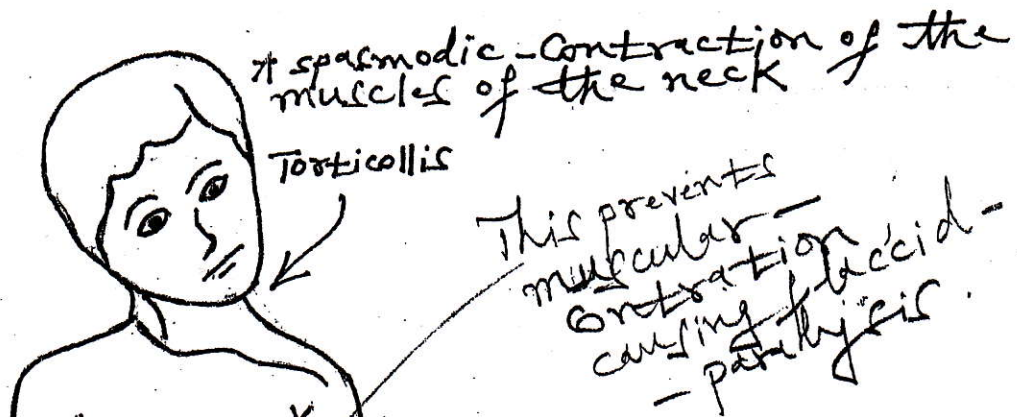
torticollis [*L. tortus*, twisted, + *collum*, neck]. Wryneck; stiff-neck; caput obstipum; rheocrania; trachelocyllosis; a contraction, often spasmodic, of the muscles of the neck, chiefly those supplied by the spinal accessory nerve; the head is drawn to one side and usually rotated so that the chin points to the other side.



Torticollis

6.1.

More of disease
in exam
what is the
+ treatment?
small quantities
of Botulinum toxin.



Pathogenesis: Botulinum toxin is absorbed from the gut and carried via the blood to peripheral synapses. Where it blocks release of acetylcholine. It is a protease that cleaves the proteins involved in acetylcholine release. The toxin is a polypeptide encoded by a lysogenic phage. Along with tetanus toxin, it is among the most powerful toxic substances ever known on earth. There are eight immunologic types of toxin: types A, B, and E are the most common in human illness. Minute amounts of the toxin are effective in the treatment of certain spasmodic muscle disorders such as torticollis and

spasmodic
winking
Wink =
sudden jerk

blepharospasm, strabismus (cross-eye) and
"down" winkles in
the center of the
forehead

contraction
of the
orbicularis-
palpebrarum -
muscle



Bacilli are $4-6 \mu\text{m} \times 0.9-1.2 \mu\text{m}$, with
OVAL, CENTRAL OR
SUBTERMINAL SPORES
GIVING THE BACILLUS
A TENNIS-RACKET-LIKE
SHAPE.

Food-borne Botulism

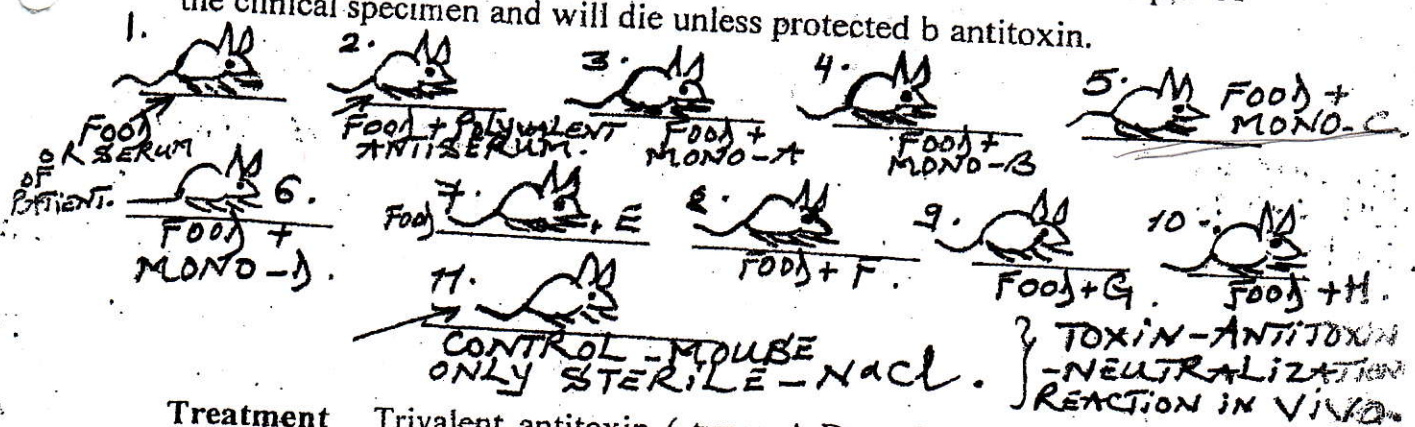
Clinical Findings Sudden onset of cranial nerve paralysis: nausea, vomiting, descending weakness and paralysis, including diplopia, dysphagia, and respiratory muscle failure and cardiac paralysis and death, are seen. No fever is present. Two special clinical forms occur ^{can} also:-
(1) wound botulism, in which spores contaminate a wound, germinate, and produce toxin at the site; and (2) infant botulism, in which the

Types of
disease
in?

* = TYPES A, B, C, D, E, F, G, AND H.
& exotoxins

organisms grow in the gut and produce toxins. Ingestion of honey containing the organism is implicated in transmission of infant botulism. Affected infants develop weakness or paralysis and may need respiratory support but usually recover spontaneously. In the United States, infant botulism accounts for about half of the cases of botulism, and wound botulism is associated with drug abuse, especially skin-popping with black tar heroin.

Laboratory Diagnosis The organism is usually not cultured. Botulinum toxin is demonstrable in uneaten food and the patients serum by mouse protection tests. Mice are inoculated with sample of the clinical specimen and will die unless protected by antitoxin.



Treatment Trivalent antitoxin (types A, B, and E) is given, along with respiratory support. The antitoxin is made in horse, and serum sickness occurs in about 15% of antiserum recipients.

Prevention Proper sterilization of all canned and vacuum packed foods is essential. Food must be adequately cooked to inactivate the toxin. Swollen cans must be discarded (clostridial proteolytic enzymes form gas, which swells cans).

* = FLACCID - PARALYSIS, NOT SPASTIC, BECAUSE SPASTIC-TYPES ARE OF CENTRAL-ORIGIN.
 متخلى، رخو

⑧ *Cl. perfringens* is sometimes found in bile, and can cause gas gangrene of abdominal muscles, following gall-bladder or bile-duct surgery especially if bile is spilled into the cavity.

3. *Clostridium Perfringens* (*C. welchii*): 60% abdominal cavity.

highly - *C. perfringens* causes two distinct diseases: gas gangrene and food poisoning.

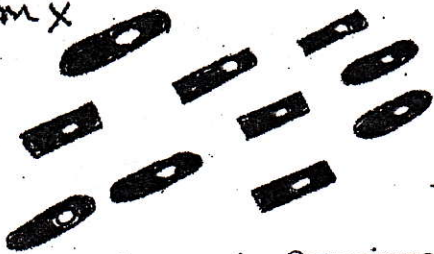
invasive.

There are 6 types of *C. perfringens* - A, B, C, D, E & F. Gas-gangrene is caused by *C. perfringens* - Type A - Heat sensitive-spores.

a. Gas Gangrene (Myonecrosis) Necrosis of muscles.

Transmission Spores are located in the soil; vegetative cells are members of the normal flora of the colon and vagina. Gas gangrene is associated with war wounds, automobile and motorcycle accidents, and septic abortions.

1-6 $\mu\text{m} \times \mu$.



BACILLI ARE LARGE WITH SQUARE OR ROUNDED ENDS, OCCURRING SINGLY OR IN PAIRS WITH NON-FULGURANT SUBTERMINAL-OVAL SPORES.

Pathogenesis Organisms grow in traumatized tissue* (especially muscle) and produce a variety of toxins. The most important is alpha - α toxin (lecithinase), which damages cell membranes, including those of erythrocytes, resulting in hemolysis. Degradative enzymes produces gas in tissues. OTHER TOXINS ARE: β - beta-toxin, epsilon - toxin; iota (i) - toxin; theta (θ) - toxin, eta (η) - toxin; kappa (κ) - toxin; lambda - λ - toxin; mu - μ - TOXIN AND NU - ν - toxin.

(E) epsilon - toxin; iota (i) - toxin; theta (θ) - toxin, eta (η) - toxin; kappa (κ) - toxin; lambda - λ - toxin; mu - μ - TOXIN AND NU - ν - toxin.

Clinical Findings Pain, edema, and cellulites occur in the wound area. Crepitation indicates the presences of gas in tissues. Hemolysis + bleeding and jaundice are common, as are blood - tinged exudates. Shock and death can ensue. Mortality rates are high.

* = PRODUCES 12 TOXINS, AND MANY ENZYMES - DNase, Hyaluronidase, 4-MAJOR TOXINS ARE IMPORTANT: α , β , ϵ and i (alpha, Beta, epsilon, AND iota).

• = CO_2 AND H_2 .

* * = TISSUE-NECROSIS, MUSCLES-NECROSIS, HEMOLYSIS OF R.B.C. DESTRUCTION OF WBC, DESTRUCTION OF PLATELETS.

PATHOGENESIS OF GAS - GANGRENE :-

1. Gas-gangrene is a polyethiological disease, caused by *Cl. perfringens* in 60%, and *Cl. oedematiens*, *Cl. bifermentans*, *Cl. histolyticum*, *Cl. fallax*, *Cl. septicum* in 40% of cases.
2. Pyogenic-cocci and Gram-negative bacteria are also infecting the wound (CONSUME Oxygen).
3. BLOOD-SUPPLY IN THE WOUND IS INTERRUPTED → "ISCHEMIA". The wound becomes ANAEROBIC.
4. ISCHEMIA LEADS TO NECROSIS (DEATH OF TISSUES)
5. DEATH OF SOFT-TISSUES, RESULTING FROM LOSS OF BLOOD-SUPPLY IS CALLED "GANGRENE".
6. LOCAL-EH (OXIDATION-REDUCTION-POTENTIAL) AND LOCAL-pH are reduced → ANAEROBIOSIS.
7. *Cl. perfringens* spores start to germinate → secrete alpha-toxin which causes: -
 - a). Degradation of lecithin in mammalian-cells
 - b). Lysis of R.B.C.
 - c). Lysis of platelets,
 - d). Destruction of W.B.C.→ secrete DNase: which degrades the viscous-DNA in necrotizing tissues or exudates, thus aiding in the spread of infection.

• 10 •

writes about myonecrosis?

- Secrete "HYALURONIDASE": which disrupts the organization of the ground-substance thus facilitating the spread of infection
- Toxins Kill cells and produce necrotic-tissues that are favorable for further anaerobic-growth.
- *Cl. perfringens* ferments tissue - carbohydrates and produce gases ($H_2 + CO_2$) → that swell the tissues and produces Crepitation on palpation : GAS-gangrene
- Butyric-butylic-fermentation of tissue carbohydrates by *Cl. perfringens* and the production of butyric-acid, is an important cause of severe-tissue-damage, and blackening of feet of gangrene.

COMPLICATIONS :-

- 1/. Profound-toxemia.
- 2/. Shock and death.
- 3/. Hemolytic - ANEMIA.
- AND) 4/. Acute RENAL-FAILURE.

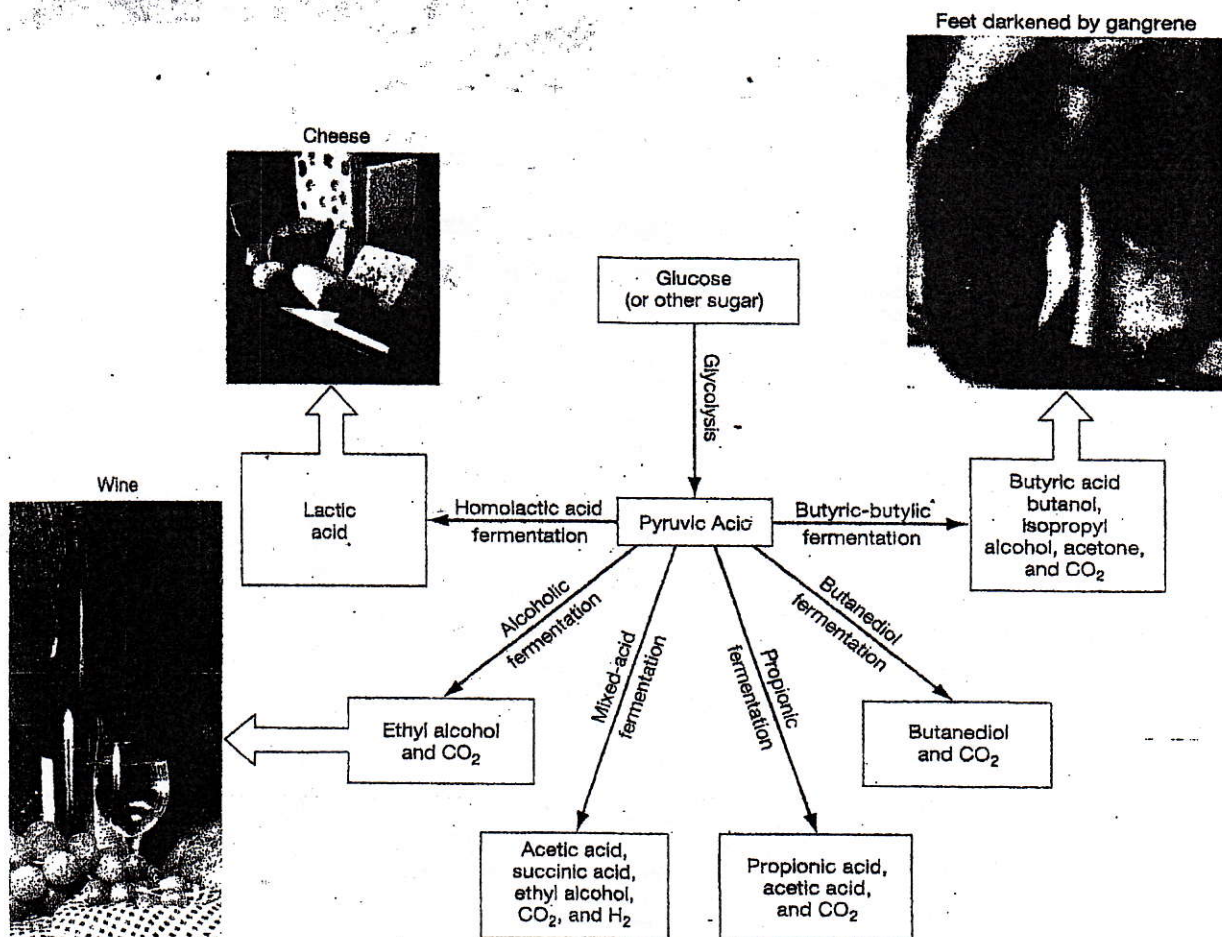
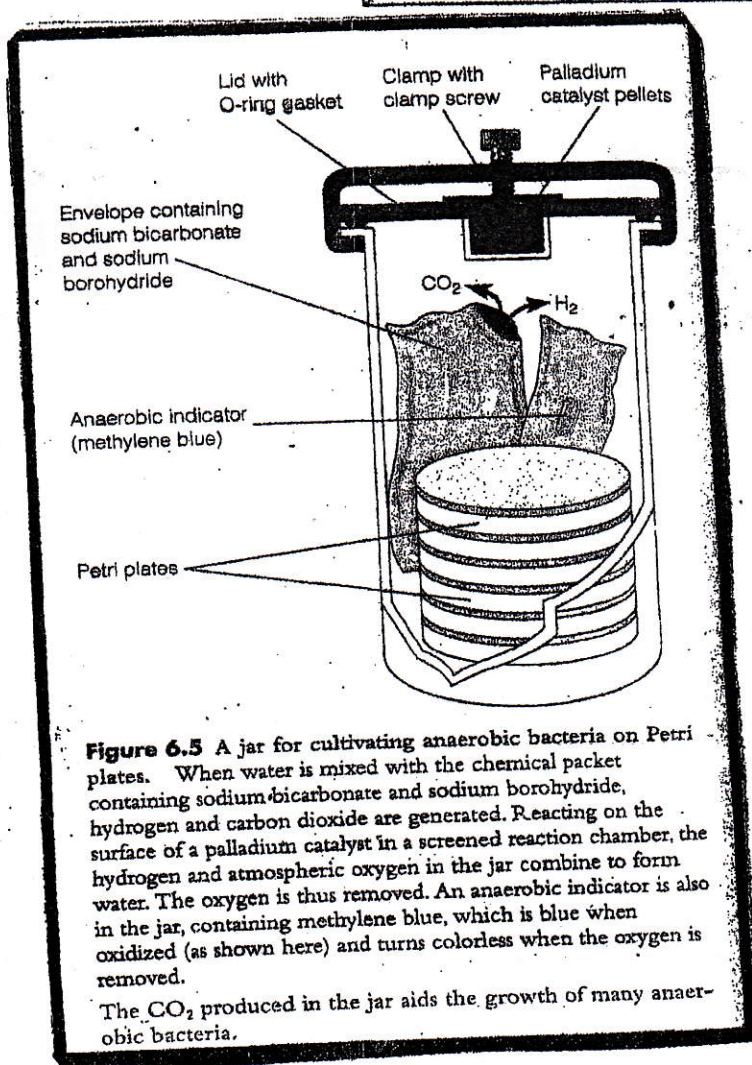
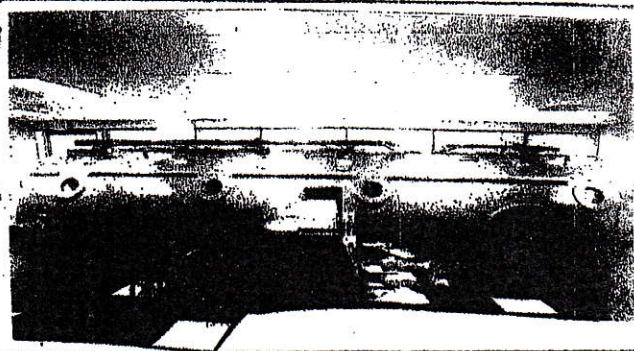


FIGURE 5.12 Fermentation pathways. Many different fermentation pathways are found among microorganisms. Would two different microbes, each fermenting a quantity of the same material necessarily produce the same products or byproducts? Flavor?

Figure 23.10 Hyperbaric chambers used to treat gas gangrene. A multiplace hyperbaric chamber that can accommodate several patients is shown. Such chambers are usually available at major medical centers.

Saturating the tissues with oxygen, in a hyperbaric chamber, prevents the growth of clostridia.



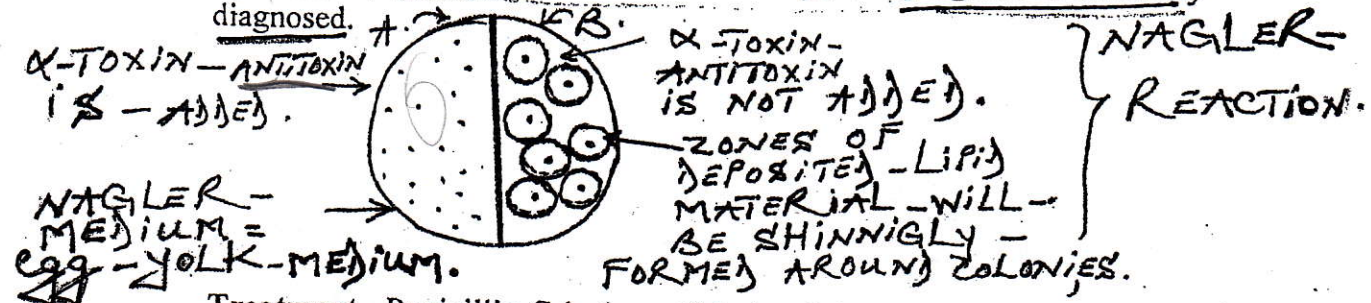
Initially diagnosed

i.e. no pus-cells,
only large-Gram-
positive rods.

① { in the absence of inflammatory cells (resulting from lysis by clostridial toxins)

Laboratory Diagnosis Smears of tissue and exudates samples show large gram - positive rods. Spores are not usually seen because they are formed primarily under nutritionally deficient by sugar fermentation reactions and acid production. C perfringens colonies exhibit a double zone of hemolysis on blood agar. Egg yolk agar is used to demonstrate the presence of the lecithinase nagler's reaction + litmus - milk - fermentation → acid + gas (++++) → gas torn the clot → stormy clot of milk. Serologic tests are not useful; gas - gangrene is clinically diagnosed.

② Anaerobic culture.



Treatment Penicillin G is the antibiotic of choice. Wounds should be debrided.

Prevention Wounds should be cleansed and debrided. Penicillin may be given for prophylaxis. There is no vaccine, ~~AND NON-RELIABLE~~ ^{ANTITOXIN}

b. Food Poisoning: is caused by C. perfringens-type - A - heat-resistant-spores!

Transmission Spores are located in soil and can contaminate food. The heat - resistant spores survive cooking and germinate. The organisms grow to large numbers in reheated foods, especially meat dishes. *. will RESIST BOILING for > 5 HOURS.
SPORES OF GAS-gangrene will NOT RESIST

Pathogenesis During sporulation (spore formation) in the gastrointestinal tract, an enterotoxin is produced. The enterotoxin is identical to a protein in the spore coat. The mode of action of the

③ IN THE FINAL-STAGE OF SPORULATION, LYSIS OF THE REMAINDER OF THE VEGETATIVE-FORM OCCURS WITH THE LIBERATION OF THE ENTEROTOXIN

Boiling for > 1-5 MINUTES.

Excellent surgical Toilet.

identical to a protein in the spore coat. The mode of action of the enterotoxin is the same as that of the enterotoxin of *S aureus*; ie, it acts as a superantigen. ✓

Clinical Findings The disease has an 8- to 16 - hour incubation period and is characterized by watery diarrhea with cramps and little vomiting. It resolves in 24 hours.

Laboratory Diagnosis This is not usually done. There is no assay for the toxin. Large numbers of the organisms can be isolated from uneaten food.

→ **C - ENTEROTOXEMIA IN SHEEP AND CATTLE**: CAUSED BY *Clostridia* - types B, C, D AND E.

D - TYPES - C AND F: CAN CAUSE → **ENTERITIS - NECROTICUS**:-

• **PREDISPOSING FACTORS**:-

- i - Malnutrition; AND small children.
- ii - pig - faeces: (source of infection).
- iii - poverty.
- iv - poor - hygienic - situation.
- v - Protein deficiency → **malnutrition** → **ENZYME** - (Trypsin)

because Trypsin inactivates the toxin.

potatoes OR secreted by *Ascaris lumbricoides*.

• **TREATMENT**: 1. Penicillin or chloramphenicol.
2. i/v fluids 3. Surgery 4. Beta-toxoid - vaccine FOR CHILDREN.

Gas gangrene is also caused by other histotoxic clostridia such as *C histolyticum*, *C septicum*, and *C novyi*, *C fallax*. (it is a polyethiological disease). : 40 %.

482



483



Enteritis Necroticans (Pigbel)

482 Appearance of intestine at operation Extensive sloughing and necrosis of the large bowel occurs in this condition which is related to infection with *Clostridium welchii* type C, due to the consumption of insufficiently cooked pork.

483 Old woman feeding her pig In the highlands of New Guinea, Enteritis necroticans is related to pig feasting which is an integral and complex part of the indigenous culture of highland tribes. The feeding of infant pigs may even take priority over the feeding of human infants.

أعياد دينية
للخنازير

الإحاطة .16.
write shortly about bigbel disease?

Treatment Symptomatic treatment is given; no antimicrobial drugs are administered.

Prevention There are no specific preventive measures. Food should be adequately cooked to kill the organism.

4. Clostridium Difficile → *difficile: Difficult; i.e. difficult to isolate difficult to grow*
Disease C difficile causes antibiotic - associated pseudomembranous colitis.

Transmission The organism is carried in the gastrointestinal tract in approximately 3% of the general population and up to 30% of hospitalized patients. C difficile is the most common nosocomial cause of diarrhea. It is transmitted by the fecal - oral route. The hands of hospital personnel are important intermediaries.

Pathogenesis Antibiotics suppress drug-sensitive members of the normal flora, allowing C difficile to multiply and produce exotoxins A and B. exotoxin A is an enterotoxin that causes an outpouring of fluid, resulting in watery diarrhea. Exotoxin B is a cytotoxin that causes damage to the colonic mucosa, leading to pseudomembrane formation. One of the diagnostic tests in the laboratory is based on the ability of exotoxin B to kill cell cultures. The mechanism of action of exotoxin B is to ADP - ribosylate a GTP-binding protein called Rho that causes depolymerization of actin in the cytoskeleton. The mechanism of action of exotoxin A is unknown.

Clindamycin was the first antibiotic to be recognized as a cause of pseudomembranous colitis, but many antibiotics are known to cause this disease. At present, **second- and third - generation**

write them
17.
+ Cefuroxime *Zinnat Zinerel*
+ ceftriaxone
+ cefotaxime
+ cefazidime
+ cefapime
+ Ampicilic

Ciprofloxacin
Norfloxacin
Levofloxacin

antagonists or synergists from medical personnel

Adenosine - 5'-diphosphate = ADP

↑
Adenosine - 5'-phosphate

↓
Guanosine - 5'-triphosphate

Guanosine - 5'-triphosphate

cephalosporins are the most common causes because they are so frequently used. In addition to antibiotics, **cancer chemotherapy** also predisposes to pseudomembranous colitis. *C. difficile* rarely invades the intestinal mucosa.

Clinical Findings *C. difficile* causes diarrhea associated with **pseudomembranes** (yellow-white plaques) on the colonic mucosa. The diarrhea is usually not bloody, and neutrophils are found in the stool in about half of the cases. The pseudomembranes are visualized by sigmoidoscopy. Toxic megacolon can occur, and **surgical resection of the colon** may be necessary.

Laboratory Diagnosis Exotoxin B is detected in filtrates of stool samples by its cytotoxic effect on cultured cells. It is identified by inhibition of cytotoxicity by specific antibody. Anaerobic culture is usually not done. An ELISA that detects both exotoxins A and B is available.

Treatment The causative antibiotic should be withdrawn. Oral metronidazole or vancomycin should be given and fluids replaced. Metronidazole is preferred because using vancomycin may select for vancomycin-resistant enterococci. In many patients, treatment does not eradicate the carrier state and repeated episodes of colitis can occur.

Prevention There are no preventive vaccines or drugs. Antibiotics should be prescribed only when necessary.

MISUSE OF ANTIBIOTICS

END

18-
الذوئيل